REMARKS

Status of Claims

In this paper, claims 4, 6-9, 12, 17, 18, 25 and 43 have been amended. Support for the amendments to the claims can be found throughout the specification and claims as filed, e.g., at page 22, lines 17-22; and page 49, lines 1-11. Claims 1-14, 17, 18, 21, 24, 25, 28, 29, 31, 32, 37-40, 42, 43, 46 and 47 are pending in the application, and claims 4-9, 12, 13, 17, 18, 25 and 43 are under examination. Claims 1-3, 10, 11, 14, 21, 24, 28, 29, 31, 32, 37-40, 42, 46 and 47 stand withdrawn from consideration.

The specification has been amended to delete embedded hyperlinks as required by the Examiner.

No new matter has been added.

The amendments to the claims (or cancellation of claims) are being made for the purpose of expediting prosecution and are made without prejudice or waiver of any subject matter thereof. Applicants reserve the right to present the original claims in this or a continuing application. No new matter has been added.

Objections to the specification and claims

Claims 4 and 25 were objected to for depending on a non-elected claim. Without agreeing with the objection, claim 4 has been rewritten as an independent claim and does not depend on a non-elected claim. Similarly, claim 25 as now pending does not depend on a non-elected claim.

Claims 12 and 18 were objected to for reciting the language “a pharmaceutical”. Without agreeing with the objection, the claims have been amended to recite the language “a pharmaceutical composition”.

The specification was objected to for containing hyperlinks. Without agreeing with the objection, the specification has been amended to delete the hyperlinks.

Applicants contend that the objections do not apply to the pending specification and claims and should be withdrawn.

Rejections under 35 U.S.C. §101

Claims 4-9, 12, 13, 17, 18, 25 and 43 stand rejected under 35 U.S.C. §101 as allegedly being directed to non-statutory subject matter. This rejection is traversed.

Without agreeing with the rejection, claims 4, 7-9, 17 and 43 have been amended to recite that the claimed polynucleotides, vectors and transformants are isolated.

Applicants respectfully contend that the pending claims meet all the requirements of, *inter alia*, 35 USC §101. Reconsideration and withdrawal of the rejection is requested.

Rejections under 35 U.S.C. §112, first paragraph (enablement)

Claims 17 and 18 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. This rejection is traversed.

First, Applicants note that the claim 17, which depends from claim 4, is directed to an antisense polynucleotide comprising a base sequence complementary to the base sequence of the polynucleotide of claim 4 (that is, a polynucleotide represented by SEQ ID NO:16, or a polynucleotide having at least 80% homology to the polynucleotide represented by SEQ ID NO:16.

Further, although the Office Action states that "problems related to therapeutic use of nucleic acids were well known in the art at the time of the invention," Office Action at page 5, Applicants contend that one of ordinary skill in the art at the time the application was filed would have been able to practice the subject matter of pending claims 17 and 18 using no more than routine experimentation.

Applicants note that the present specification describes the claimed antisense polynucleotides and how to make them. Moreover, the specification provides

examples, including working examples, of the use of certain antisense polynucleotides to reduce expression of certain proteins and/or cause apoptosis in cancer cells (see, e.g., Examples 2, 19, 20 and 21). Thus, the present application provides extensive guidance in making and using the subject matter of claims 17 and 18.

Still further, Applicants submit herewith copies of references showing that use of antisense polynucleotides was well established at the time the present application was filed (these references are also cited on the Information Disclosure Statement attached hereto). For example, Valesky et al. ("Noninvasive Dynamic Fluorescence Imaging of Human Melanomas Reveals that Targeted Inhibition of bFGF or FGFR-1 in Melanoma Cells Blocks Tumor Growth by Apoptosis", *Molecular Medicine* (2002) 8(2): 103-112) discloses, *inter alia*, that injection of antisense constructs into tumors *in vivo* (in a mouse model) caused "massive apoptosis" of tumor cells and largely halted growth of tumor volume. In another example, Kamiyama et al. ("VEGF receptor antisense therapy inhibits angiogenesis and peritoneal dissemination of human gastric cancer in nude mice", *Cancer Gene Therapy* (2002) 9: 197-201) showed that an antisense construct inhibited tumor cell proliferation *in vitro*, and inhibited tumor dissemination and induced tumor cell apoptosis *in vivo* (in a mouse model).

In a still further example (published subsequent to the filing of the present application), Koller et al. ("Use of a Chemically Modified Antisense Oligonucleotide Library to Identify and Validate Eg5 (Kinesin-Like 1) as a Target for Antineoplastic Drug Development", *Cancer Res.* (2006) 66(4): 2059-2066) discloses that an antisense construct caused cell cycle arrest and/or apoptosis of breast cancer cells *in vitro*, and administration of an antisense construct *in vivo* (in a mouse model) resulted in a "statistically significant reduction in tumor growth" (page 2064, left column) with "[n]o apparent toxic effects" (page 2064, right column).

The references discussed above show that administration of antisense constructs in amounts effective to cause tumor cell apoptosis and inhibit growth of tumors (including human tumor cell lines) *in vivo* was well-known to one of ordinary skill in the art at the time the present application was filed. In view of the teachings of the present specification and the state of the art at the time the application was filed,

Applicants contend that one of ordinary skill in the art, at the time the application was filed, would have been able to make and use the claimed antisense polynucleotides and pharmaceutical compositions using no more than routine experimentation.

Applicants respectfully contend that the specification provides enablement for the full scope of the pending claims, and, furthermore, that the pending claims meet all the requirements of, *inter alia*, 35 USC §112. Reconsideration and withdrawal of the rejection is requested.

Rejections under 35 U.S.C. §102(b)/(e)

Claims 4-9, 12, 13, 17 and 18 stand rejected under 35 U.S.C. §102(b)/(e), as allegedly anticipated by the Williams et al. reference. This rejection is traversed.

Pending claims 4-9, 12, 13, 17 and 18 are directed to an isolated polynucleotide comprising a polynucleotide represented by SEQ ID NO:16, or a polynucleotide having at least 80% homology to the polynucleotide represented by SEQ ID NO:16 (claims 4-6); a pharmaceutical composition comprising such a polynucleotide (claim 12); a diagnostic agent comprising such a polynucleotide (claim 13); an isolated recombinant vector comprising such a polynucleotide (claim 8); an isolated transformant transformed by the recombinant vector (claim 9); an isolated antisense polynucleotide comprising a base sequence complementary to the base sequence of such a polynucleotide (claim 17); a pharmaceutical composition comprising such an antisense polynucleotide (claim 18); and a polynucleotide consisting of the base sequence represented by SEQ ID NO: 16 (claim 7).

The Williams reference does not disclose an isolated polynucleotide comprising a polynucleotide represented by SEQ ID NO:16, or a polynucleotide having at least 80% homology to the polynucleotide represented by SEQ ID NO:16, or a polynucleotide consisting of the base sequence represented by SEQ ID NO: 16. The Williams reference also does not disclose vectors, transformants, pharmaceutical compositions, or diagnostic agents as presently claims, nor does Williams disclose an isolated antisense polynucleotide complementary to the base sequence of SEQ ID NO:16 or

pharmaceutical compositions thereof. Therefore, the Williams reference does not and cannot anticipate the pending claims.

Claims 4-7 and 17 stand rejected under 35 U.S.C. §102(b), as allegedly anticipated by the GenBank (EST) Accession No. BQ68095. This rejection is traversed.

The GenBank reference does not disclose an isolated polynucleotide comprising a polynucleotide represented by SEQ ID NO:16, or a polynucleotide having at least 80% homology to the polynucleotide represented by SEQ ID NO:16, or a polynucleotide consisting of the base sequence represented by SEQ ID NO: 16. The GenBank reference also does not disclose an isolated antisense polynucleotide complementary to the base sequence of SEQ ID NO:16. Therefore, the GenBank reference does not and cannot anticipate the pending claims.

Reconsideration and withdrawal of the rejections is proper and is requested.

Rejection under 35 U.S.C. §103(a)

Claims 25 and 43 stand rejected under 35 U.S.C. §102(b)/(e), as allegedly unpatentable over the Williams et al. reference in view of Croce et al., U.S. Patent No. 5,928,884. This rejection is traversed.

Pending claim 25 is directed to a kit for screening a compound or its salt inhibiting the expression of a gene, the kit comprising the polynucleotide according to claim 4 (i.e., a polynucleotide represented by SEQ ID NO:16, or a polynucleotide having at least 80% homology to the polynucleotide represented by SEQ ID NO:16). Pending claim 43 is directed to a kit for screening a prophylactic/therapeutic agent for a cancer, the kit comprising an isolated polynucleotide according represented by SEQ ID NO:16, or a polynucleotide having at least 80% homology to the polynucleotide represented by SEQ ID NO:16).

The disclosure of the Williams reference have been discussed above. The Croce reference is cited in the Office Action only for teaching a "diagnostic kit comprising a DNA probe as an active ingredient." In view of the differences between

the Williams reference and the subject matter of claims 25 and 43, the William reference cannot render obvious claims 25 and 43 (and the Office Action does not suggest otherwise). Applicants contend that the Croce reference – which also does not disclose a polynucleotide represented by SEQ ID NO:16, or a polynucleotide having at least 80% homology to the polynucleotide represented by SEQ ID NO:16 - cannot "bridge the gap" between the teachings of the Williams reference and the subject matter of the pending claims. Because neither the Williams reference nor the Croce reference, alone or in combination, render obvious any pending claim, the rejection cannot stand and should be withdrawn.

CONCLUSION

Early and favorable consideration of the application is earnestly solicited.

If the Examiner considers that obstacles to allowance still exist, the undersigned invites the Examiner to contact him at the telephone number given below.

Applicants conditionally petition for any further extension of time required. The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 62936 (46342).

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Respectfully submitted,

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